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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/654,112	09/02/2003	Tassie Collins	018781-008610US	4775

7590 02/23/2006

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EXAMINER	
SACKEY, EBENEZER O	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/654,112	COLLINS ET AL.	
	Examiner	Art Unit	
	EBENEZER SACKEY	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36,80,83 and 84* is/are pending in the application.

4a) Of the above claim(s) *3,5,6 and 10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7-9,13-36,80,83 and 84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/02/03,10/04/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-36, 80 and 83-84 are pending.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Information Disclosure Statement

Receipt of the Information Disclosure Statement filed 09/02/03 and 10/04/05 respectively is acknowledged. Signed copies of the 1449 are attached herewith.

Response to Restriction Requirement

Applicant's election of species of Example 12 is acknowledged. In response to applicants request in view of the restriction requirement mailed on 11/25/05, the following request has been granted, i.e., the restriction has been reformulated as such: R^1 and R^2 are selected from H, halogen, CN, CO_2R, C_{1-8}alkyl, CONR'R".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-9, 21-22, 24-26, 13-30, 34-36, 80, 83 and 84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of asthma, atomic dermatitis, HIV infection, atherosclerosis, multiple sclerosis and rheumatoid arthritis associated with CCR4 receptor activity, does not reasonably provide enablement for the treatment of diseases mediated by CCR4 receptor activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim. The treatment of diseases mediated by CCR4 activity is not properly supported in the specification. The specification fails to adequately teach how to use the invention properly by failing to provide enabling disclosure regarding the above diseases. Because of the high level of unpredictability associated with chemical or biological systems, a greater amount of evidentiary support is needed in order to fully

satisfy the requirement of 35 USC 112, first paragraph, that applicants provide sufficient guidance as regards "how to use" the invention. For example, it is not clear what is encompassed by "CCR4 mediated condition or disease."

Applicants need to point out in the specification where there is support including pharmaceutical data for the alleged utility. A mere statement does not provide enabling support for such a utility.

The nature of the invention relates to methods of treating diseases or conditions mediated by the activity of CCR-4 receptors. However, the claims are not enabled, based solely on specification's description that instant compounds have activity as CCR-4 receptor antagonists or agonists. No clear evaluation of their relevance to *in vivo* efficacy for any one use is ever set forth and no actual test data has been reported. See *In re Stevens,* 16 USPQ 2d. 1379 regarding sole reliance on description of testing protocol.

There is no known magic bullet for the treatment of all diseases associated with CCR4 activity. The amount of guidance provided in found on page 44 wherein TARC and/or MDC binding to CCR4 is provided without any reference to a specific disease associated with CCR4 disorders. As stated above, the state of the art is that there is no known treatment medication for all diseases associated with CCR4. See Schwartz et al., which discloses the current treatable diseases associated with instant mode of action. The specification provides no other guidance as to what other diseases are being treated by the administration of the instant compounds. The notion that thiazolyl derivatives of formula (I) that are anti CCR4 agents, the activity relied on herein, have such a range of uses is not seen in the art at the time of applicants' effective filing or

even in the present. There is no evidence of record that there is a correlation of success for the disclosed diseases let alone the treatment of all those diseases. The list of CCR4 mediated diseases constitutes "an invitation to experiment" which is not in compliance with 35 USC 112.

Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects". Thus, in the absence of a showing of correlation between all the diseases claimed as capable of being mediated by compounds of formula (I), one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds of formula (I) due to the unpredictability of the art. Claims 21, 22, 24, 25, 26, 35, and 36 are also rejected because there is no data in the specification, which clearly correlates innate immunity, septic shock, platelet aggregation, thrombosis, myocardial infarction, allergic condition and cancer to the instant receptors. Thus, in the absence of any correlation between studies conducted *in vitro* and the diseases to be treated, there is no sufficient evidence to support the claimed uses.

Inventions targeted for human therapy bear a particular heavy responsibility to provide supporting data because of the unpredictability in biological responses to therapeutic treatment. Also, the standard of enablement is higher of such inventions simply because effective treatments for disease conditions are relatively rare, and may be prima facie unbelievable in the absence of strong supporting data. See *Exparte Stevens*, 16 USPQ 2d 1379 (BPAI) in which a prima facie case of nonenablement against a method of treating cancer was affirmed based solely on legal precedents. See also *Ex Parte Chwang,* 231 USPQ 751 (BPAI) 1986 and *Ex Parte Krepelka,* 231 USPQ 746 (BPAI) 1986.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4, 7-9, 13-14, 18, 21, 23-24, 25, 27-36, 80, 83 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what a CCR4 mediated condition is. Additionally, CCR4 mediated condition is of indeterminate scope because defining disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since, the claim language may read on diseases not yet known to be caused or effected by such action or in ways not yet know.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4, 7-9, 13-30, 32-36, 80, 83 and 84 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 82-83, 85-91, 96-122 of co-pending U.S. Patent Application No. 2003/0018022 A1 ('022'). Although the conflicting claims are not identical, they are not patentably distinct from each other because there is substantial overlap between methods of using compounds of structural formula (I) and derivatives thereof and that of co-pending 2003/0018022 A1. The reference of '022' discloses for the same purpose compounds, which generically correspond to compounds employed in instant methods. See for example claims 80 and 83 respectively.

The instant claims differ from '022' in the generic description of the compounds, i.e., for example where W is a substituted or unsubtituted naphthyl whereas '022' teaches among others aryl and where X is S etc.

The claimed invention would be obvious from the use of similar compounds of the reference in treating various disease state such as multiple sclerosis absent of any unobvious or unexpected properties especially since one of ordinary skill in the art would expect that structurally similar compounds would have the same or virtually the same properties. This is nothing more than the extension of monopoly. The motivation to make the invention derives from the expectation that structurally similar compounds would possess similar activity.

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-2, 4, 7-9, 13-33, 36, 80, 83 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Musser et al., (4,826,990).

Applicants claim a CCR4 inhibitor compounds for treating various disease states, such as asthma, the substituents are as defined in claim 1 and elsewhere.

Determination of the scope and content of the prior art (MPEP §2141.01)

Musser et al., disclose the use of similar compounds with similar utility (i.e. treating asthma etc). See the entire reference, especially column 1, lines 1-9, column 2, lines 1-65 and Example 14, which differs from the instant compounds in the generic description of the compounds employed in treating the various disease states.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between compounds employed in the prior art and the compounds instantly employed is that of generic description. The indiscriminate selection of "some" among "many" is *prima facie* obvious. *In re Lemin,* 141 USPQ 814 (1964). Additionally, Musser et al., provides the necessary teaching and guidance to arrive at the instantly claimed compounds. *In re Baird, 29 USPQ 2d. 1550 (1994) CAFC.* Note the reference teaches the treatment of rheumatoid arthritis, column 11, lines 25-26, bronchial asthma, line 40-42.

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)

The motivation to make the claimed compounds derives from the expectation that compounds structurally similar to instant compounds would possess similar activity (i.e., for example treating asthma).

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art to prepare CCR4 inhibitor compounds as disclosed by Musser et al., with a reasonable expectation of success absent a showing of unexpected results. Therefore, at the time of filing this application, one of ordinary skill in the art in possession of Musser et al., would have been in possession of the instant method of use absent a showing of unexpected results and/or properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (571) 272-0704. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

EOS
February 14, 2006

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